CHAPTER 1

Principles of surgical oncology

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Surgical oncology, as its name suggests, is the specific application of surgical principles to the oncologic setting. These principles have been derived by adapting standard surgical approaches to the unique situations that arise when treating cancer patients.

The surgeon is often the first specialist to see the patient with a solid malignancy, and, in the course of therapy, he or she may be called upon to provide diagnostic, therapeutic, palliative, and supportive care. In each of these areas, guiding paradigms that are unique to surgical oncology are employed.

In addition, the surgical oncologist must be knowledgeable about all of the available surgical and adjuvant therapies, both standard and experimental, for a particular cancer. This enables the surgeon not only to explain the various treatment options to the patient but also to perform the initial steps in diagnosis and treatment in such a way as to facilitate and avoid interfering with future therapeutic options.

Invasive diagnostic modalities

As the surgeon approaches the patient with a solid malignancy or abnormal nodal disease or the rare individual with a tissue-based manifestation of a leukemia, selection of a diagnostic approach that will have a high likelihood of a specific, accurate diagnosis is paramount. The advent of high-quality invasive diagnostic approaches guided by radiologic imaging modalities has limited the open surgical approach to those situations where the disease is inaccessible, a significant amount of tissue is required for diagnosis, or a percutaneous approach is too dangerous (due, for example, to a bleeding diathesis, critical intervening structures, or the potential for unacceptable complications, such as pneumothorax).

Lymph node biopsy

The usual indication for biopsy of the lymph node is to establish the diagnosis of lymphoma or metastatic carcinoma. Each situation should be approached in a different manner.

Lymphoma The goal of biopsy in the patient with an abnormal lymph node and suspected lymphoma is to make the general diagnosis and to establish the lymphoma type and subtype. Additional analyses of the cells in the node, its internal architecture, and the subpopulations of cells are critical for subsequent treatment. Although advances in immunocytochemical and histochemical analyses have been made, adequate tissue is the key element in accurate diagnosis.

Consequently, the initial diagnosis of lymphoma should be made on a completely excised node that has been minimally manipulated to ensure that there is little crush damage. When primary lymphoma is suspected, the use of needle aspiration does not consistently allow for the complete analyses described above and can lead to incomplete or inaccurate diagnosis and treatment delays.

When recurrent lymphoma is the primary diagnosis, the analysis of specific cell type is very important for assessing changes in the type of lymphoma and whether a transformation has occurred. In the rare situation in which recurrent Hodgkin's disease is suspected, a core biopsy may be adequate if the classic Reed-Sternberg cells are identified. However, in the initial and recurrent settings, biopsy of an intact node is often required.

Carcinoma The diagnosis of metastatic carcinoma often requires less tissue than is needed for lymphoma. Fine-needle aspiration (FNA), core biopsy, or subtotal removal of a single node will be adequate in this situation. For metastatic disease, the surgeon will use a combination of factors, such as location of the node, physical examination, and symptoms, to predict the site of primary disease. When this information is communicated to the pathologist, the pathologic evaluation can be focused on the most likely sites so as to obtain the highest diagnostic yield. The use of immunocytochemical analyses can be successful in defining the primary site, even on small amounts of tissue.

Head and neck adenopathy The head and neck region is a common site of palpable adenopathy that poses a significant diagnostic dilemma. Nodal zones in this area serve as the harbinger of lymphoma (particularly Hodgkin's disease) and as sites of metastasis from the mucosal surfaces of the upper aerodigestive tract, nasopharynx, thyroid, lungs, and, occasionally, from intra-abdominal sites, such as the stomach, liver, and pancreas.

Since treatment of these nodal metastases varies widely, and since subsequent treatments may be jeopardized by inconveniently placed biopsy incisions, the surgical oncologist must consider the most likely source of the disease prior to performing the biopsy. FNA or core biopsy becomes a very valuable tool in this situation, as the tissue sample is usually adequate for basic analysis (cytologic or histologic), and special studies (eg, immunocytochemical analyses) can be performed as needed.

Biopsy of a tissue-based mass

Several principles must be considered when approaching the seemingly simple task of biopsying a tissue-based mass. As each of the biopsy methods has unique

risks, yields, and costs, the initial choice can be a critical factor in the timeliness and expense of the diagnostic process. It is crucial that the physician charged with making the invasive diagnosis be mindful of these factors.

Mass in the aerodigestive tract In the aerodigestive tract, biopsy of a lesion should include a representative amount of tissue taken preferably from the periphery of the lesion, where the maximum amount of viable malignant cells will be present. Since the treatment of in situ and invasive disease varies greatly, the biopsy must be of adequate depth to determine penetration of the tumors. This is particularly true for carcinomas of the oral cavity, pharynx, and larynx.

Breast mass Although previously a common procedure, an open surgical biopsy of the breast is rarely indicated today. Palpable breast masses that are highly suspicious (as indicated by physical findings and mammography) can be diagnosed as malignant with close to 100% accuracy with FNA. However, because the distinction between invasive and noninvasive disease is often required prior to the initiation of treatment, a core biopsy, performed either under image guidance (ultrasonography or mammography) or directly for palpable lesions, is the method of choice.

An excellent example of the interdependence of the method of tissue diagnosis and therapeutic options is the patient with a moderate-sized breast tumor considering breast conservation who chooses preoperative chemotherapy for downsizing of the breast lesion. The core biopsy method establishes the histologic diagnosis, provides adequate tissue for analyses of hormone-receptor levels and other risk factors, causes little or no cosmetic damage, does not perturb sentinel node analyses, and does not require extended healing prior to the initiation of therapy. In addition, a small radio-opaque clip can be placed in the tumor to guide the surgical extirpation. This is important because excellent treatment responses can make it difficult for the surgeon to localize the original tumor site.

Mass in the trunk or extremities For soft-tissue or bony masses of the trunk or extremities, the biopsy technique should be selected on the basis of the planned subsequent tumor resection. The incision should be made along anatomic lines in the trunk or along the long axis of the extremity. When a sarcoma is suspected, FNA can establish the diagnosis of malignancy, but a core biopsy will likely be required to determine the histologic type and plan neoadjuvant therapy.

Preoperative evaluation

As with any surgical patient, the preoperative evaluation of the cancer patient hinges primarily on the individual's underlying medical condition(s). Because most new cancers occur in older patients, careful attention must be paid to evaluation of cardiovascular risks. Adequate information can usually be obtained from a standard history, physical examination, and electrocardiogram (ECG), but any concerns identified should be subjected to a full diagnostic work-up.

The evaluation should also include a detailed history of current and previous therapies. Many patients will be on anticoagulation, aspirin, or analgesics, all of which may impact on their perioperative management. Previous use of doxorubicin may be associated with cardiac dysfunction and the use of bleomycin with severe lung sensitivity to oxygen concentrations > 30%.

Prior radiation therapy is associated with fibrosis and delayed healing. An appreciation of potential postoperative problems secondary to these factors is important in planning the surgical extirpation and reconstruction. For example, in a patient who requires mastectomy after failed breast-conserving surgery, the zone of tissue damage from the original radiation therapy can be assessed by reviewing the port and boost site films or by examining the irradiated site for tattoo marks used to align the radiation field. Plans for resection of heavily irradiated tissues should be made preoperatively in concert with the reconstructive surgeon, and the relative increased risk of postoperative problems should be discussed with the patient. This evaluation should include the type of tissue to be transferred, analysis of potential donor and recipient sites and vessels, and assurance that the appropriate microvascular equipment is available, in the event that it is needed during surgery.

Pathologic confirmation of the diagnosis

The treatment of cancer is based almost exclusively on the organ of origin and, to a lesser degree, on the histologic subtype. Unless the operative procedure is being performed to make a definitive diagnosis, review of the pathologic material is needed to confirm the diagnosis preoperatively.

There are few exceptions to this doctrine, and it behooves the surgeon to have a confirmed diagnosis, including the in situ or invasive nature of the cancer, prior to performing an operation. This tenet assumes paramount importance when one is performing procedures for which there is no recourse once the specimen is removed, eg, laryngectomy, mastectomy, removal of the anal sphincter, and extremity amputation.

Ironically, in some situations, a preoperative or intraoperative diagnosis cannot be confirmed, despite the fact that the preoperative and intraoperative physical findings, laboratory data, and radiologic studies (pre- and intraoperative) overwhelmingly suggested the cancer diagnosis. The classic example of this dilemma is the jaundiced patient with a firm mass in the pancreatic head. The Whipple procedure (pancreaticoduodenectomy) causes significant morbidity but is required to make the diagnosis and treat the cancer. In any of these situations, the preoperative discussion with the patient must include the possibility that the final diagnosis may be a benign lesion.

Resection

The principles of resection for malignant disease are based on the surgical goal (complete resection vs debulking), functional significance of the involved or-

gan or structure, and the ability to reconstruct the involved and surrounding structures. Also important are the technical abilities of the surgeon or availability of a surgical team, adequacy of neoadjuvant and adjuvant therapies, and the biologic behavior (local and systemic) of the disease. Although "operable" is used to describe the physiologic status of the patient, the definition of "resectable" varies, and this term can be defined only in the context of the aforementioned modifying parameters.

Wide excision

A wide excision includes the removal of the tumor itself and a margin of normal tissue, usually exceeding 1 cm in all directions from the tumor. The margin is variable in a large, complex (multiple tissue compartments) specimen, and the limiting point of the resection is defined by the closest approximation of cancerous tissue to the normal tissue that is excised.

Wide margins are recommended for tumors with a high likelihood of local recurrence (eg, dermatofibrosarcoma protuberans) and for tumors without any reliable adjuvant therapeutic options.

Breast The use of adjuvant radiation therapy has permitted the use of breast-conserving surgery, which limits the excision of wide margins of normal breast tissue.

Colon and rectum For carcinoma of the colon and rectum, the width of excision is defined by the longitudinal portion of the bowel and the inclusion of adjacent nodal tissue. The principles of wide resection require removal of normal bowel (including at least 5 cm of uninvolved tissue), the associated mesenteric leaf, and adjacent rectal soft tissue (mesorectum).

This general principle has been modified in the distal rectum, where lateral margins are maintained using the principles of mesorectal excision and longitudinal bowel margins of 2 cm are accepted. This modification reflects the emphasis on functional results (ie, maintenance of anal continence) and the availability of adequate adjuvant (pre- or postoperative) radiation therapy to improve local control.

No touch technique

This principle is based on the concept that direct contact with and manipulation of the tumor during resection can lead to an increase in local implantation and embolization of tumor cells, respectively. Theoretically, the metastatic potential of the primary lesion would be enhanced by the mechanical extrusion of tumor cells into local lymphatic and vascular spaces. There may be some validity to this theory with respect to tumors that extend directly into the venous system (eg, renal cell tumors with extension to the vena cava) or those that extensively involve local venous drainage (eg, large hepatocellular carcinomas).

Extensive palpation and manipulation of a colorectal primary have been shown to result in direct shedding of tumor cells into the lumen of the large bowel. The traditional strategy to lessen this risk was to ligate the proximal and distal

lumen of the segment containing the tumor early in the resection. These areas were then included in the resection, limiting the contact of shed tumor cells with the planned anastomotic areas.

Neither of the previous theoretical situations (ie, manipulation of the tumor and direct contact of the tumor with the anastomotic area) has been definitively tested in controlled, prospective, randomized trials. Therefore, the risk-benefit ratio should favor adherence to the general principles of minimal tumor manipulation, protection of the anastomotic areas, and exclusion of the resection bed from potential implantation with tumor cells if the surgeon is to include them in performing the operation.

The introduction of minimally invasive surgical techniques approximately 15 years ago was incorporated into the surgical procedures for a non-oncologic scenario—cholecystectomy, hiatal and inguinal hernia repair, and treatment of benign diseases of the female reproductive tract. Transfer of the technology to the oncologic setting was met with resistance, as questions of technical (number of nodes resected and less tactile input during resection) and therapeutic (local control, disease-free survival, and overall survival) equivalence were raised.

Careful clinical research has answered these initial reservations for colon cancer. Results from a recently published, prospective randomized trial reported by the Laparoscopic Colectomy (LC) Trial group documented that although the laparoscopic operations took longer than the open procedures (150 vs 95 minutes), there was no difference in the margins obtained, the 30-day mortality, or the complication rate. LC resulted in a shorter overall hospital stay (4 vs 5 days) and less use of parenteral narcotics (3 vs 4 days) than the open procedure. There was no difference identified for the oncologic outcomes of disease-free recurrence or overall survival.

Examples in colon cancer will serve as paradigms for the study of other tumors. Expansion of minimally invasive techniques, with preservation of oncologic principles and improvement in patients' quality-of-life outcomes, will drive surgical interventions.

Lymphadenectomy

Early surgical oncologic theory proposed that breast cancer progressed from the primary site to the axillary lymph nodes to the supraclavicular nodes and nodes of the neck. This theory led to the radical surgical approach that included resection of all of the breast tissue and some or all of the above-noted draining nodal basins (ie, modified radical, radical, or extended radical mastectomy).

Absent from this approach was an appreciation of the nodes not only as a deposit of regional metastatic disease but also as a predictor of systemic disease. Modern treatment approaches view nodal dissection as having a triple purpose: the surgical removal of regional metastases, the prediction of prognosis, and the planning of adjuvant therapy.

The surgical technique and boundaries for lymphadenectomy are based on nodal basins that are defined by consistent anatomic structures. For example, dissection of the neck is defined by the mandible, anterior strap muscles of the

neck, clavicle, trapezius muscle, carotid artery, vagus nerve, brachial plexus, and fascia overlying the deep muscles of the neck.

Modifications of classic techniques Each of the classic anatomic lymphadenectomies has been modified along lines that consider the predicted positivity and functional impact of the dissection. To use the example of radical neck dissection, the modifications include supraomohyoid dissection for tumors of the floor of the mouth (a high-risk zone) and sparing of the spinal accessory nerve (functional prevention of shoulder drop and loss of full abduction of the shoulder).

As alluded to in the previous paragraphs, lymph node dissection has therapeutic value only in patients with positive nodes. In individuals with pathologically negative nodes, the benefit is limited to prediction of prognosis and documentation of pathologic negativity. Therefore, in the pathologically negative nodal basin, there is minimal benefit to outweigh the risks and untoward sequelae of the dissection.

Sentinel node biopsy

Technique The technique of sentinel node identification has been developed to address clinically negative nodal basins. With this technique, the node or nodes that preferentially drain a particular primary tumor are identified by mapping and then surgically excised. The mapping agents include radiolabeled materials and vital dyes that are specifically taken up by, and transported in, the lymphatic drainage systems. These mapping and localizing agents, used alone or in combination, are critical in defining the unique flow patterns to specific lymph node(s) and ambiguous drainage patterns (eg, a truncal melanoma that may drain to the axilla, supraclavicular, or inguinal spaces).

Unresolved issues As this field of directed diagnostic node biopsy and dissection develops, many technical issues related to the timing and location of the injections are being evaluated. In addition, the type of pathologic evaluation (ie, the number of sections examined per node and the use of immunohistochemical analysis) is undergoing intense scrutiny.

A study of 200 consecutive patients who had sentinel lymph node biopsies performed for breast cancer examined the concepts of injecting dye and radioactive tracer into either the breast or the overlying dermis. The authors believed that the technical aspects of intradermal injection were simpler and more easily reproduced than those of injections into the breast. Injections were performed in group 1 intraparenchymally and in group 2 intradermally. The combination of blue dye and isotope localization produced a 92% success rate in group 1 and a 100% success rate in group 2. The authors concluded that dermal and parenchymal lymphatics of the breast drain to the same lymph node, and that the more simple approach of dermal injection may simplify and optimize sentinel lymph node localization.

For melanoma, for which these techniques were originally developed, researchers are studying the feasibility and clinical relevance of evaluating nodal material with polymerase chain reaction (PCR) techniques. These techniques are also being

studied in breast cancer, where the clinical relevance (indication for adjuvant therapy) of the presence of micrometastases or PCR-only metastases is highly controversial and, therefore, questions the need for this intense level of pathologic scrutiny.

Elective lymph node dissection has limited value in intermediate-thickness melanoma. In clinically node-negative patients, the use of the sentinel node technique can avoid postoperative complications, increase confidence about the better prognosis, and avoid the significant side effects of adjuvant immunologic therapy. However, the identification of histologically positive nodes via sentinel node biopsy is expected to have significant benefit, as it will result in a complete therapeutic dissection and adjuvant therapy with interferon-α (Intron A, Roferon-A). In contrast, for patients with sentinel node–positive breast cancer, the value of completing a level I, II axillary node dissection is uncertain. This important question is being examined in two national, prospective clinical trials.

Palliation

In the continuum of care for the cancer patient, aspects of palliation, or the reduction of suffering, are delegated to the surgeon. This text includes many examples of palliative surgical procedures: venous access, surgical relief of ascites with shunt procedures, neurosurgical intervention for chronic pain, fixation of pathologic fractures, and placement of feeding tubes to deliver food and medications. The surgeon must be versed in the techniques of and indications for such interventions and discuss their risks and benefits with the patient, caregivers, and referring physician. The barriers to the initiation and practice of palliative surgery include the reluctance of patients, family, and referring physicians; health care system administrative obstacles; and cultural factors. A "therapeutic index" (time spent receiving treatment for symptoms vs time symptom free) should be constructed and discussed during the benefit/risk, informed consent process.

Resuscitation issues An ethical issue of resuscitation must be addressed when considering palliative surgical intervention. Some may take the position that if a patient is to have surgery, he or she must be willing to undergo full resuscitation if required. That tenet may be set aside in the palliative setting, in which the operative intervention is planned only to relieve suffering. In such a case, a frank discussion with the patient and appropriate family members can avoid the distressing situation of the patient being placed on unwanted, fruitless life support. Again, the surgeon is called upon not only to provide a technical service but also to achieve a comprehensive understanding of the disease process and how it affects each individual cancer patient.

SUGGESTED READING

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